Effects of Toxic Exposure to Molds and Mycotoxins in Building-Related Illnesses

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ABSTRACT. The authors studied 100 patients who had been exposed to toxic molds in their homes. The predominant molds identified were *Alternaria, Cladosporium, Aspergillus, Penicillium, Stachybotrys, Curvularia,* Basidiomycetes, Myxomycetes, smuts, *Epicoccus, Fusarium, Bipolaris,* and *Rhizopus.* A variety of tests were performed on all, or on subgroups of, these patients. Sensitivities and exposures were confirmed in all patients by intradermal skin testing for individual molds (44–98% positive), and by measurement of serum antibodies. Abnormalities in T and B cells, and subsets, were found in more than 80% of the patients. The findings of trichothecene toxin and breakdown products in the urine, serum antibodies to molds, and positive intradermal skin tests confirmed mycotoxin exposure. Respiratory signs (e.g., rhinorrhea, sinus tenderness, wheezing) were found in 64% of all patients, and physical signs and symptoms of neurological dysfunction (e.g., inability to stand on the toes or to walk a straight line with eyes closed, as well as short-term memory loss) were identified in 70% of all patients. Objective abnormal autonomic nervous system tests were positive in all 100 patients tested. Brain scans, conducted using triple-head single photon emission computed tomography, were abnormal in 26 (86%) of 30 (subgroup of the 100) patients tested. Objective neuropsychological evaluations of 46 of the patients who exhibited symptoms of neurological impairment showed typical abnormalities in short-term memory, executive function/judgment, concentration, and hand/eye coordination.
<Key words: immunological, mold, mycotoxin, neurological>

TOXIC EXPOSURE to molds and mycotoxins in public buildings, office buildings, and homes is becoming commonplace. In the current study, 2 adults in each of 31 families (n = 62), plus an additional 38 "solo" individuals who lived alone (n = 2) or had no other family members affected (n = 36), had been exposed to mold in their own homes or apartments. These patients reported symptoms of respiratory, neurological, and immune dysfunction. (Children were not included in this study.)

Materials and Method

A total of 100 patients (61 females, 39 males; age range 21–78 yr; mean age 44.3 yr) were studied to determine the health effects of the presence of toxic molds in their homes. Their houses were analyzed by an independent professional mold evaluator to determine the type and duration of mold exposure that had occurred. All patients had to vacate their homes, at least

during the period of remediation, and 10 left their homes permanently because of health concerns.

Signs and symptoms were recorded for each organ system by an examining physician. Mold and mycotoxin sensitivity were confirmed by positive skin whealing with intradermal serial dilution titration and/or the intradermal provocation method.[1–3] Immune abnormalities were confirmed by individual T- and B-cell counts, which were performed by flow cytometry.[4] Immune globulin was evaluated by the mold antibody assay (i.e., immunoglobulin [Ig]G, IgM, IgA, and IgE) method of Vojdani et al.,[5] and urine trichothecenes were measured by the method of Croft.[6] Delayed recall antigens were measured 48 hr postinjection to assess cell-mediated immunity,[7] using testing kits (Multi-Test® II) supplied by Lincoln Diagnostics, Inc. (Decatur, Illinois). The autonomic nervous system was evaluated by the pupillography method of Ishikawa et al.[8] and by the heart rate variability method of Riftine.[9,10]

Neuropsychological tests, performed in accordance with the method of Butler et al.,[11] were conducted by Dr. Didriksen. Brain scans were performed by Dr. Simon, using single-photon emission computed tomography in conjunction with a triple-head gamma camera (tripleSPECT), which provides imaging of the tracer distribution in 3 dimensions.[12] Scans were analyzed in accordance with the method of Simon.[13]

Results

Signs and symptoms. The predominant signs and symptoms observed in our subjects were as follows: (a) respiratory symptoms (i.e., sneezing, rhinorrhea, nasal stuffiness, dyspnea, and wheezing) in 64 patients; (b) neurological symptoms (short-term memory loss, imbalance, and dizziness) in 70 patients; (c) immunological symptoms (hypersensitivity to molds, foods, and chemicals) in 100 patients; (d) gastrointestinal symptoms (i.e., bloating, gas, and cramps) in 24 patients; (e) musculoskeletal symptoms (i.e., muscle and joint aches and tenderness) in 29 patients; and (f) cardiovascular symptoms (bruising, hemoptysis, and petechiae) in 10 patients.

Indoor mold cultures. The common molds found in the 69 homes analyzed represented a wide spectrum of molds. Results of the indoor mold cultures are given in Table 1.

Intradermal sensitivity testing. Each individual's mold and mycotoxin sensitivity and exposure were confirmed by intradermal injection with preservative-free antigens. Negative controls for saline were nonreactive, except in 5% of the patients, whereas positive controls for histamine were positive in all patients (Table 2). Intradermal skin test results for individual molds in the 100 patients showed reactions that varied from 44% to 98% positive results (Table 2). All patients reacted to at least 4 molds; therefore, 100% of the patients reacted to skin testing. The remaining 45 tests were also positive for the Ascomycetes molds *Leptosphaeria* (98%) and *Phaesophaeria* (98%). A comparison group of 30 patients, 21–60 yr of age, who were selected for moderate sensitivity to molds and who did not receive massive exposures, showed 20% positive intradermal tests for molds.

Table 1.—Indoor Mold Cultures Taken from 69 Homes*

Mold type	No. of homes	Percentage of homes
Alternaria	68	100
Aspergillus/Penicillium	68	100
Cladosporium	68	100
Stachybotrys	55	80
Epicoccus	55	80
Curvularia	54	79
Basidiomycetes	52	76
Myxomycetes	51	75
Smut	50	73
Fusarium	50	73
Bipolaris	46	67
Rhizopus	45	65

Source: Environmental Health Center–Dallas, Dallas, Texas, 2003, Bertie Griffiths, Ph.D.
*Two adults per house in 31 houses (= 62 individuals) + 1 person in each of 38 homes (not every mold found in each home). Average clean house = 0–4 fungal colonies per culture.

For subgroups of the studied patients, intradermal tests for aflatoxin were positive for 21 of 27 (79%); 25 of 25 (100%) tested positive for trichothecene; and 22 of 24 (91%) tested positive for *Fusarium*. These intradermal tests were compared with those for the aforementioned 30 normal controls, of whom 1% were positive. (This intradermal test was developed relatively recently and thus was unavailable for the first 75–78 patients studied because its efficacy and safety were not verified until later in the study period.)

Immune parameters. White blood cell counts were abnormal in 11% of the 100 patients, and the total lymphocyte count was decreased in 23% of patients (Table 3). CD_{11} counts (i.e., total T_{11}-cells) were low in 29 patients, and high in 4, of the 100 patients studied. CD_4 counts (i.e., T_4-helper cells) were low in 32% of the patients and high in 40% of the patients. CD_8 counts (i.e., T_8-suppressor cells) were low in 22% of patients and high in 11%. B_4 lymphocyte counts were abnormal in 14% of the patients: elevated in 11% and depressed in 3%.

Cell-mediated immunity for delayed recall antigens (*Proteus*, tuberculin, *Candida*, *Streptococcus*, *Staphylococcus*, diphtheria, and tetanus) was positive for 3 or fewer antigens in 59 (71%) of 83 patients measured (Table 3). A cell-mediated immunity of 3 or less was considered abnormal. Nineteen patients were not mea-

Table 2.—Intradermal Mold Provocation/Neutralization Testing (*N* = 100 Patients)

Mold, mycotoxin, toxic metabolite, or algae	Patients			Comparison group			
				Avg. mold-sensitive		Nonsensitive	
	Positive	Tested	Percentage positive	Positive	Tested	Positive	Tested
Rhizopus	89	100	89	30	100	1	30
Aspergillus mix	81	84	96	20	100	2	30
Penicillium	89	100	89	5	100	1	30
Trichoderma	79	90	88	20	100	1	30
Cladosporium herbarum	75	79	95	25	100	2	30
Stachybotrys	75	87	86	30	100	3	100
Curvularia spp.	73	77	95	10	100	4	30
Sporobolmyces	71	84	85	5	100	1	30
Streptomyces	68	70	97	10	100	0	30
Monilia situ	68	75	91	5	100	0	30
Drechslera	68	77	88	5	100	1	30
Cladosporium fulvum	63	72	88	2	100	0	30
Leptosphaeria	61	62	98	2	100	1	30
Phaesophaeria	44	45	98	2	100	3	30
Lake algae	83	84	99	3	100	0	30
Aflatoxin	21	27	79	4	30	1	30
Fusarium	22	24	91	0	30	0	30
Trichothecene	25	25	100	6	30	1	30

Source: Environmental Health Center–Dallas, Dallas, Texas, 2003.

Table 3.—Major Immune Parameters (*N* = 100 Patients)

Cell type	Control range (*n* = 60)	Abnormal (%)	
		Increase	Decrease
White blood cells	4,000–11,0000	2	9
Lymphocytes	1,200–3,300	7	23
T_{11}	1,000–4,000	4	29
T_4	657–1,770	40	32
T_8	325–1,050	11	22
T_4/T_8	1–2.7	21	5
B_4	82–477	11	3
Cell-mediated immune response†		71%	59/83

Source: Environmental Health Center–Dallas, Texas; 2003.
*More than 1 abnormality per patient.
†3 or less was considered abnormal. *Proteus*, tuberculin, *Candida*, *Streptococcus*, *Staphlycoccus*, diphtheria, tetanus, and delayed recall at 48 hr. Nineteen percent of the patients did not have delayed recall antigens measured because of unavailability of the testing solution.

sured because the laboratory was unable to provide recall antigens.

Serum mold antibody assays. Table 4 contains the results obtained for 100 patients for mold and mycotoxin antibodies in serum, including IgA, IgG, IgM, IgE, and Vojdani's reference ranges.[5] These serum mold antibody results were correlated with those for the positive intradermal skin tests, and were also compared with Vojdani's controls.[5] The number of patients with massive mold exposures exceeded controls for at least 4 molds, and often for as many as 10.

Trichothecene urine testing. Tests for trichothecene and its byproducts in urine were completed in accordance with the method of Croft.[6] Urine was collected and analyzed approximately 6 mo (range = 1–12 mo) after patients evacuated their homes. Not all of our subjects underwent this testing because the assay was not available at the beginning of the study. Of the 78 patients tested, 9 were in the "present but low" (3–4 units) category, 30 were in the "moderate" (5–8) category, and 39 were in the "high positive" (9+) category. These findings were compared with values determined for recovered, treated patients (0–2).

Comparison between positive urine mycotoxins and positive trichothecene serum antibodies revealed a 98% correlation in the 78 patients measured. One patient who had anaphylaxis had mycotoxins in urine; however, this patient also had negative serum antibodies. All of the urine specimens that were positive for mycotoxins (i.e., in the high, moderate, or low categories) correlated with positive mycotoxin skin tests; however, only 27 patients received mycotoxin skin tests, given the more recent development of the tests. Of the other patients who had positive tests for serum mycotoxin antibodies, 8 were positive for IgA to molds, 8 were positive for IgG to molds, and 6 were positive for IgM to molds. These 22 patients had no urine mycotoxins measured because the test was unavailable, inasmuch as the laboratory experienced difficulties in handling the volume of tests. Three patients were positive for IgE to molds, but none of these had urine measurements done.

Table 4.—Blood Mold Antibody Assay (N = 100 Patients)*

Mold or mycotoxin	IgA Elevated (n)	IgA Tested (n)	IgA %	IgG Elevated (n)	IgG Tested (n)	IgG %	IgM Elevated (n)	IgM Tested (n)	IgM %	IgE Elevated (n)	IgE Tested (n)	IgE %	Nonsensitive	Controls
Aspergillus fumigatus	4	21	19	9	21	43	5	21	24	4	21	19	0	1,600
Aspergillus niger	23	82	28	22	82	27	25	82	30	10	32	12	0	1,600
Aspergillus versicolor	6	17	35	6	17	35	2	17	12	2	17	12	0	1,600
Alternaria tenuis	4	48	8	19	48	40	14	48	29	6	48	13	0	1,600
Chaetomium globosum	11	42	26	16	42	38	15	42	36	7	42	17	0	1,600
Chrysagem	0	1	0	0	1	0	0	1	0	0	1	0	0	50
Cladosporium herbarum	12	67	18	25	67	37	20	67	30	8	67	12	0	1,600
Epicoccum nigrum	7	26	27	25	67	37	20	67	30	8	67	12	0	1,600
Fumigatus	0	2	0	0	2	0	0	2	0	0	2	0	0	1,600
Fusarium nachilform	0	2	0	0	2	0	0	2	0	0	2	0	0	1,600
Geotrichum candidiolum	0	6	0	2	6	33	1	6	17	0	6	0	0	1,600
Penicillium notatum	10	84	12	35	84	42	19	84	23	9	84	11	0	1,600
Rhizopus nigrans	2	9	22	7	9	78	6	9	67	1	9	11	0	1,600
Stachybotrys chartarum	16	85	19	35	85	41	28	85	33	13	85	15	0	1,600
Aflatoxins	26	92	28	26	92	28	35	92	38	15	92	16	0	1,600
Satratoxins	21	88	24	27	88	31	26	88	30	13	88	15	0	1,600
Trichothecene	32	88	36	38	88	43	27	88	31	10	88	11	0	1,600

Source: Environmental Health Center–Dallas, Dallas, Texas, 2003.
Notes: Immunoglobulin (Ig) E was significantly lower than IgG, IgM, IgG, and IgM. Ig levels determined by Vodjani, Immunosciences Laboratories, Beverly Hills, California.
*Not all individuals had the same assay, given the differences in findings in each home.

Autonomic nervous system measurements. Evaluation of autonomic nervous system function via eye pupillography[8] was performed in 58 patients and revealed abnormalities in 51, whereas 7 patients tested normal (Table 5A). These results revealed significant changes in the pupillary area (A_1), the constriction ratio (CR) of the pupillary area before and after a light challenge of 400 lux (A_3/A_1), and the speed of contraction (T_2) after a light challenge of 400 lux. Recovery time (T_5) showed no significant change.

Autonomic nervous system measurements via heart rate variability[9,10] were performed on 67 mold/mycotoxin-exposed patients, compared with 65 controls. Abnormalities were revealed in all patients (Table 5B). A comprehensive fitness score—including sympathetic–parasympathetic function with frequency recordings, the amount of microcirculation vasoconstriction, and the chronophoric reaction of the heart—was markedly elevated in all 67 patients measured (score = 10.16) compared with 65 controls (score = 6.06). The patients' scores were significantly abnormal ($p < 0.001$) and indicated autonomic nervous system impairment.

There was overlap in the 2 measurement methods in that 25 patients were administered both tests. The 7 patients who had a normal pupillography also had a heart rate variability change, and we considered them "positive" for the study.

Neurocognitive data. Neurocognitive data for 46 (65%) of the 70 neurotoxic patients (mean age = 47.95 yr, mean educational level = 15.32 yr) who reported massive mold/mycotoxin exposures were examined in the present study. Because of financial limitations, in some cases multiple familial neurocognitive recordings were not performed on members of the same family (i.e., husband and wife combining time in the same household), and it was this that contributed to the discrepancy in numbers of untested patients. Neuropsychological test batteries of varying comprehensiveness (including the Halstead-Reitan Neuropsychological Test Battery) were compared with normative data. Deficits were found primarily on measures of executive function, psychomotor problem-solving, and incidental memory. Scores on the Wechsler Memory Scale-III were within normal limits overall, with greatest impairment

Table 5.—Autonomic Nervous System Testing*

A. Pupillography†

Pupillary change parameters	Patients (n = 58) $\bar{x}$	Patients (n = 58) SD	Controls (n = 181) $\bar{x}$	Controls (n = 181) SD	Difference‡
A_1 (mm²)	26.91	1.62	35.10	1.59	$p < 0.001$
CR (A_2/A_1) (mm²)	0.29	0.01	0.46	0.03	$p < 0.001$
T_2 (ms)	269.6	5.6	199.0	5.2	$p < 0.001$
T_5 (ms)	1,616	83	1,414	70	$p < 0.05$

B. Heart Rate Variability§

	Patients (n = 67)	Controls (n = 65)	Difference
Fitness score	10.16	6.06	$p < 0.001$

Notes: $\bar{x}$ = mean, SD = standard deviation, A_1 = pupillary area, CR (A_2/A_1) = constriction ratio of the pupillary area before and after a light challenge of 400 lux, T_2 = speed of contraction after a light challenge of 400 lux, and T_5 = recovery time.
*Some patients were administered both tests (n = 25).
†Method: Ishikawa, Hamamatsu Photonics, Hamamatsu City, Japan.[8]
‡p values < 0.001 were significant.
§Method: Riftine, Heart Rhythm Instruments, Inc., Metuchen, New Jersey.[10]

on measures of visual memory. Fifty-seven percent of the 70 patients demonstrated mild to moderate impairment on the Halstead-Reitan Battery. Forty-two percent demonstrated mild to severe impairment on the Comprehensive Neuropsychological Screen, and an additional 17 percent scored in a low-normal range. Scores on measures of specific neuropsychological abilities showed some impairment of sensory and motor functions. Intelligent Quotient scores generally fell within expected ranges.

Brain scans. TripleSPECT brain scans of 30 patients, selected randomly for physical signs of imbalance, revealed a neurotoxicity pattern in 26 (86%). All 100 patients could not be evaluated because of cost constraints. Of the 26 with a neurotoxicity pattern, 15 individuals displayed mild neurotoxicity and 11 showed moderate neurotoxicity. In the glutathione-dependent areas of the cerebral hemispheres, the patterns showed a decrease in flow and function, temporal lobe asymmetry, and a flow of dye into soft tissue with areas of high dye uptake ("hot" areas) or no dye uptake ("cold" areas). Further details of tripleSPECT brain scans are contained in a study by Simon and Rea.[12]

Discussion

All patients received the same skin, blood, and autonomic nervous system tests, whereas , for financial reasons, a selected subgroup underwent the tripleSPECT brain scan, urine mycotoxin, and intradermal mycotoxin tests. Subgroup testing did not appear to bias the study, but confirmed the initial findings because of the high correlation. Clearly, toxic mold in our patients' homes was associated with adverse health effects in this series of patients. The 62 individuals of the 31 families appeared to have a more severe exposure than did the 38 solo patients inasmuch as multiple individuals in the same home were made ill. The individuals who lived alone (n = 2) or had no family members affected (n = 36) had histories similar to the families who were affected, but for an unknown reason only 1 member of this group was ill. However, in these 38 solo patients, the intensity of exposure (i.e., countable colonies vs. too numerous to count) appeared to be less than in the 62 family members. These findings could be related to the different lengths of time (3 mo to 2 yr) spent in the home, as well as the intensity of growth of the mold cultures. Given that mold counts are crude and have large variations in reported mold quantity, abnormalities in counts may have occurred and may have resulted in more exposure—even if patients were exposed to the same antigen. Even if the mold counts were the same, perhaps the less-damaged patients did not spend as much time in their homes (thus less exposure) as did the more severely damaged patients, or perhaps these individuals had more resistance to mold exposures. Alternatively, perhaps the mold/mycotoxin growth was not as vigorous or virulent as in the homes in which more than 1 patient was made ill. Technology to evaluate quantitative mycotoxin exposure and virulence is unavailable, making these parameters difficult to evaluate.

Water leakage that leads to mold growth involves leaking roofs and windows, and other water-related defects in structures (e.g., defective construction with

leaking showers, sewer pipes, water pipes). The multiplicity of molds found in homes appeared to cause a total body load (burden) dyshomeostasis—as evidenced by the multiplicity of positive skin tests, pan immune sensitivity, and autonomic dysfunction which occurred alternatively or simultaneously in any given patient. Not only did the total burden of the mold load appear significant, but damage from a *specific* mold—up to 10 separate categories—also appeared to occur. One mold (*Stachybotrys*) and 1 mycotoxin (trichothecene) seemed particularly virulent, damaging all 3 systems: immune, respiratory, and neurological. A larger spectrum of many other molds not listed or considered pathogenic was found in the serum antibodies and skin tests of most patients, as well as in several individual homes and cases. These additional molds may also create a greater total body burden, which may aid in disrupting the immune and detoxification systems, thus augmenting the damage caused by the predominant molds. This additive or synergistic effect of multiple molds might also have caused the more severe disease seen in the massively exposed patients.

Another reason that most patients developed a near pan-sensitivity could have been the frequency of exposure. The molds commonly found in patients' homes were those typically found outdoors, like *Alternaria*, *Aspergillus*, and *Cladosporium*, whereas *Stachybotrys* is usually found indoors. These particular molds could cause specific sensitivity and toxicity, as well as trigger various aspects of the immune and detoxification systems—regardless of the patient's location. This phenomenon would tend to exacerbate one's illness once sensitization occurred. Clearing of symptoms would be difficult inasmuch as there would be minimal avoidance time from exposure to the triggering agent because exposure events occurred both indoors and outdoors.

Judging by the mycotoxins or breakdown products found in urine (in all 78 patients tested), antibodies (found in 99 of 100 patients tested in this category), and positive intradermal skin tests of a small subgroup of 27 patients tested for mycotoxins (i.e., aflatoxin [78%], fusarium [92%], trichothecene [100%]), there appears to be strong evidence of mycotoxin exposure. These patients did not respond clinically as the average mold-sensitive patient would, or as controls with no mold sensitivity would—the symptoms of the massively exposed group were much more widespread in our study. In addition to nasal, sinus, and bronchial symptoms, the exposed group had more neurological (70 of 100 patients) and immune system (100% vs. 20% controls) involvement. Not only were their laboratory findings more frequently and severely abnormal, but clinically these mold/mycotoxin-exposed patients were much sicker. Many became incapacitated and were unable to work. This contrasted with the average mold-sensitive patient (without a massive exposure) who typically can continue to work and has the usual symptoms related only to the respiratory system (e.g., rhinosinusitis, asthma, cough).

Parameters suggestive of more severe problems than just an average mold sensitivity included alterations in white blood cell count (in 19% of patients), alterations in T-lymphocyte subsets of helper cells (72%), changes in T_8 lymphocytes (33%), and changes in B lymphocytes (24%). These findings further substantiate that the immune system was significantly altered in these patients with massive mold/mycotoxin exposure. Cell-mediated immunity decreased in 71% of 83 patients measured, again pointing to abnormal T-cell function. It appears that the mycotoxin overload significantly disrupted the immune system of these severely exposed patients.

A high correlation was seen between the number of molds to which a patient was exposed (4+ per patient) and (a) their total immunoglobulin changes (100% change) and (b) the number of positive skin tests (44–98% [Table 2]). When tested intradermally, patients with massive mold/mycotoxin exposure demonstrated almost a pan sensitivity to these molds found on culture, and to other molds not found on culture. This finding contrasted with the average mold-sensitive patient who has sensitivities to only 20% of the molds tested. The finding of pan mold sensitivity suggested a severe alteration in both the immunological and neurological systems. Such a severe immunological reaction would likely trigger the autonomic system because of the close anatomical proximity and physiologic communication of the autonomic nerves. These alterations of both the nerves and immune cells may have resulted in a vulnerability to exposure from other molds in the ambient outdoor air and indoor air—not necessarily just the molds found in their immediate home exposures. Recognition sites on cell membranes might also have been damaged as a result of the severe reactions—or the harmonious function of the T-helper and T-suppressor cells might have been disrupted—thus allowing pan sensitivity to occur in these patients.

Neurological involvement from mold/mycotoxin exposures was evidenced not only by abnormal physical findings (i.e., inability to stand on toes with the eyes closed or to walk a straight line), but also by the abnormal results in objective measurements of autonomic nervous system dysfunction and by tripleSPECT brain scan results. An imbalance in the autonomic nervous system certainly emphasizes that there is a proven communication between the central nervous system and the immune system. Autonomic abnormalities occurred in virtually all of our patients, which suggests that mold/mycotoxin sensitivity and overload initially caused a basic change in the nervous system, which could then propagate some of the sympathetic and parasympathetic effects we saw in these patients. Alternatively, the au-

tonomic nervous system change might have occurred later in the course of illness (no patients were measured until 3 mo following exposure) as a result of long-term exposure and ongoing reactions. The comparison groups with mild, average mold sensitivity exhibited very few autonomic dysfunctions.

Positive tripleSPECT brain scans (n = 26), combined with neuropsychological profiles, helped to objectively differentiate aberrations in cognition, recall, and executive function. The neurological and psychological tests correlated well with the tripleSPECT scans and autonomic tests to demonstrate a highly significant organic damage pattern. Although the number of tripleSPECT scans performed was low, the data were sufficient to allow correlation of outcomes with the autonomic and immune data. These findings suggest that direct toxic damage resulted from mold or mycotoxin exposure, or from an immunological overlay, as discussed earlier.

Our study (along with those of other investigators) has shown that systems other than respiratory system are affected in patients with massive mold/mycotoxin exposure. Gray et al.,[14] Kilburn,[15] and Campbell et al.,[16] independently, have demonstrated both immunological and neurological involvement secondary to large mold/mycotoxin exposures. Although none of these investigators conducted skin testing, their findings in regard to the home environment, clinical signs and symptoms, and serum antibodies were similar to those of our study. Correlations were found with a "toxic" building, high levels of mold cultures, and their patients' illnesses. Incapacitating factors of the mycotoxin- and mold-induced symptoms in their and our studies included short-term memory loss and inability to concentrate. The neurological involvement seen in our series, which caused patients to miss work or school and often prevented them from performing even manual tasks, appeared to be the result of mold- and mycotoxin-induced chronic fatigue. Patients found it difficult to move from their homes because of this fatigue, even though evacuation was necessary for their survival.

In summary, 100 patients exposed to toxic molds and mycotoxins in their homes were evaluated by various means (with subgroups receiving additional skin and urine testing for mycotoxins). Signs and symptoms reported were related primarily to the respiratory tract and to the neurologic and immune systems; other systems were also involved, although to a lesser degree. Serum antibodies, direct urine measurement, and intradermal skin tests for mold sensitivity demonstrated a high correlation with exposure and with alteration of the immune system. Objective alteration of the neurologic system was found by autonomic nervous system testing through the eye and heart nerves, by brain tripleSPECT scans that confirmed clinical neurological involvement, and by neuropsychological tests for memory loss, executive dysfunction, and hand/eye coordination.

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Submitted for publication September 20, 2003; revised; accepted for publication December 9, 2003.

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References

1. Rinkel HJ. Inhalant Allergy. Pt I: The whealing response of the skin to serial dilution testing. Ann Allergy, 1949; 7: 625–30.
2. Lee CH. Allergy Neutralization: The Lee Method. St. Joseph, MO: Tri Sigma Press, 1987.
3. Miller JB. Food Allergy: Provocative Testing and Injection Therapy. Springfield, IL: Charles C. Thomas, 1972.
4. Givan AL (Ed). Flow Cytometry—First Principles. New York: Wiley-Liss, 1992.
5. Vojdani A, Campbell AW, Kashanian A, et al. Antibodies against molds and mycotoxins following exposure to toxigenic fungi in a water-damaged building. Arch Environ Health 2003; 58(6):324–36.
6. Croft WA, Jastromski BM, Croft AL, et al. Clinical confirmation of trichothecene mycotoxicosis in patient urine. J Environ Biol 2002; 23(3):301–20.
7. Popa V, Holgate ST, Salvi S. Cell-mediated immunity in asthma. Am J Respir Crit Care Med 2002; 166:1607.
8. Ishikawa S, Natio M, Inabe KI. A new videopupillography. Opthalmologica 1970; 160:248.
9. Gu HG, Ren W, Lu QS, et al. Application of degree of complexity in heart rate variability analysis during orthostatic (correction of orthostatic) standing [in Chinese]. Space Med Med Eng (Beijing) 2001; 14(3):192–95.
10. Riftine A. Quantitative Assessment of the Autonomic Nervous System Based on Heart Rate Variability Analysis. Heart Rhythm Instruments, Inc., 173 Essex Ave., Metuchen, NJ 08840.
11. Harrell EH, Butler JR, Didriksen NA, et al. Harrell-Butler Comprehensive Neuropsychological Screen [unpublished assessment instrument]. Health Psychology/Behavioral Medicine Associates, 100 N Cottonwood Dr., Ste. 106, Richardson, TX 75080, 1986.
12. Simon TR, Rea WJ. Use of functional brain imaging in the evaluation of exposure to mycotoxins and toxins encountered in Desert Storm/Desert Shield. Arch Environ Health 2003; 58(7):406–09.
13. Ross GH, Rea WJ, Johnson AR, et al. Neurotoxicity in single photon emission computed tomography brain scans of patients reporting chemical sensitivities. Toxicol Ind Health 1999; 15:415–20.
14. Gray MR, Thrasher JD, Crago R, et al. Mixed mold mycotoxicosis: immunological changes in humans following exposure in water-damaged buildings. Arch Environ Health 2003; 58(7):410–20.
15. Kilburn KH. Indoor mold exposure associated with neurobehavioral and pulmonary impairment: a preliminary report. Arch Environ Health 2003; 58(7):390–98.
16. Campbell AW, Thrasher JD, Madison RA, et al. Autoantibodies and neurophysiologic abnormalities in patients exposed to molds in water-damaged buildings. Arch Environ Health 2003; 58(8). Forthcoming.